

APPENDIX A

Claims marked for amendment.

~~Strikethrough~~ indicates deletion and underlining indicates insertion.

38. (Four Times Amended) A method of screening for modulators of a lipopolysaccharide mediated response comprising the steps of:

- a) obtaining a cell expressing a TLR-4 polypeptide having the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:98 or SEQ ID NO:99;
- b) providing to the cell lipopolysaccharide sufficient to induce a lipopolysaccharide mediated response;
- ~~b~~c) measuring a lipopolysaccharide mediated response mediated by the TLR-4 polypeptide;
- ~~e~~d) contacting the TLR-4 polypeptide with a putative modulator;
- ~~d~~e) assaying for a change in the lipopolysaccharide mediated response; and
- ~~e~~f) comparing the lipopolysaccharide mediated responses mediated by the TLR-4 polypeptide obtained in steps ~~b~~c) and ~~d~~e) above

wherein a difference in the lipopolysaccharide mediated responses indicates that the putative modulator is a modulator of a lipopolysaccharide mediated response.

APPENDIX B

Clean copy of the claims as amended in U.S. Ser. No. 09/396,985.

38. A method of screening for modulators of a lipopolysaccharide mediated response comprising the steps of:

- a) obtaining a cell expressing a TLR-4 polypeptide having the amino acid sequence of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:98 or SEQ ID NO:99;
- b) providing to the cell lipopolysaccharide sufficient to induce a lipopolysaccharide mediated response;
- c) measuring a lipopolysaccharide mediated response mediated by the TLR-4 polypeptide;
- d) contacting the TLR-4 polypeptide with a putative modulator;
- e) assaying for a change in the lipopolysaccharide mediated response; and
- f) comparing the lipopolysaccharide mediated responses mediated by the TLR-4 polypeptide obtained in steps c) and e) above

wherein a difference in the lipopolysaccharide mediated responses indicates that the putative modulator is a modulator of a lipopolysaccharide mediated response.

40. The method of claim 39, wherein the lipopolysaccharide mediated response mediated by the TLR-4 polypeptide is determined by determining the ability of the TLR-4 polypeptide to stimulate transcription of a reporter gene, the reporter gene operatively positioned under control of a nucleic acid segment comprising a promoter from a TLR-4 gene.

52. The method of claim 38, wherein said putative modulator is effective in altering the mediation of the lipopolysaccharide mediated response by TLR-4.

53. The method of claim 52, wherein said putative modulator is an agonist.
54. The method of claim 52, wherein said putative modulator is an antagonist.
55. The method of claim 52, wherein said putative modulator affects the transcription of TLR-4.
56. The method of claim 52, wherein said putative modulator affects the translation of TLR-4.
57. The method of claim 38, wherein the TLR-4 polypeptide has the amino acid sequence of SEQ ID NO:2.
58. The method of claim 38, wherein the TLR-4 polypeptide has the amino acid sequence of SEQ ID NO:4.
59. The method of claim 38, wherein the TLR-4 polypeptide has the amino acid sequence of SEQ ID NO:6.
60. The method of claim 38, wherein the TLR-4 polypeptide has the amino acid sequence of SEQ ID NO:98.
61. The method of claim 38, wherein the TLR-4 polypeptide has the amino acid sequence of SEQ ID NO:99.
63. The method of claim 38, wherein said putative modulator inhibits TLR-4 directed signaling of TNF secretion.
64. The method of claim 38, wherein said putative modulator stimulates TLR-4 directed signaling of TNF secretion.

65. The method of claim 38, wherein said putative modulator to be screened is obtained from a library of synthetic chemicals.
66. The method of claim 38, wherein said putative modulator to be screened is obtained from a natural source.
67. The method of claim 65, wherein said natural source is selected from the group consisting of animals, bacteria, fungi, plant sources and living marine samples.
68. The method of claim 38, wherein said putative modulator to be screened is a protein or peptide.
70. The method of claim 38, wherein said putative modulator to be screened is a nucleic acid molecule.
71. The method of claim 38, wherein said putative modulator to be screened is a stimulator of an immune response.
72. The method of claim 71, wherein said stimulator of an immune response is a cytokine.
73. The method of claim 71, wherein said stimulator of an immune response is an interferon.
74. The method of claim 38, wherein said TLR-4 polypeptide is encoded by a nucleic acid sequence selected from the group comprising SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:46, SEQ ID NO:47 and SEQ ID NO:48.
75. The method of claim 38, wherein said putative modulator to be screened is an IL-1 receptor antagonist.